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Introduction: Mirtazapine is a noradrenergic and serotonergic antidepressant mainly acting through blockade of presynaptic **alpha-2** receptors. Published data on pregnancy outcome after exposure to mirtazapine are scarce. This study addresses the risk associated with exposure to mirtazapine during pregnancy.

Patients (or Materials) and Methods: Multicenter (n = 11), observational prospective cohort study comparing pregnancy outcomes after exposure to mirtazapine with 2 matched control groups: exposure to any selective serotonin reuptake inhibitor (SSRI) as a disease-matched control group, and general controls with no exposure to medication known to be teratogenic or to any antidepressant. Data were collected by members of the European Network of Teratology Information Services (ENTIS) during individual risk counseling between 1995 and 2011. Standardized procedures for data collection were used in each center.

Results: A total of 357 pregnant women exposed to mirtazapine at any time during pregnancy were included in the study and compared with 357 pregnancies from each control group. The rate of major birth defects between the mirtazapine and the SSRI group did not differ significantly (4.5% vs 4.2%; unadjusted odds ratio, 1.1; 95% confidence interval, 0.5–2.3, $P = 0.9$). A trend toward a higher rate of birth defects in the mirtazapine group compared with general controls did not reach statistical significance (4.2% vs 1.9%; OR, 2.4; 95% CI, 0.9–6.3; $P = 0.08$). The crude rate of spontaneous abortions did not differ significantly between the mirtazapine, the SSRI, and the general control groups (9.5% vs 10.4% vs 8.4%; $P = 0.67$), neither did the rate of deliveries resulting in live births (79.6% vs 84.3% in both control groups; $P = 0.15$). However, a higher rate of elective pregnancy-termination was observed in the mirtazapine group compared with SSRI and general controls (7.8% vs 3.4% vs 5.6%; $P = 0.03$). Premature birth (<37 weeks) (10.6% vs 10.1% vs 7.5%; $P = 0.38$), gestational age at birth (median, 39 weeks; interquartile range (IQR), 38–40 in all groups; $P = 0.29$), and birth weight (median, 3320 g; IQR, 2979–3636 vs 3230 g; IQR, 2910–3629 vs 3338 g; IQR, 2967–3650; $P = 0.34$) did not differ significantly between the groups.

Conclusion: This study did not observe a statistically significant difference in the rate of major birth defects between mirtazapine, SSRI-exposed, and nonexposed pregnancies. A slightly higher rate of birth defects was, however, observed in the mirtazapine and SSRI groups compared with the low rate of birth defects in our general controls. Overall, the pregnancy outcome after mirtazapine exposure in this study is very similar to that of the SSRI-exposed control group.

Disclosure of Interest: None declared.

OC004—FETAL EXPOSURE TO NONSTEROIDAL ANTIINFLAMMATORY DRUGS (NSAID) AND SPONTANEOUS ABORTIONS

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Introduction: Spontaneous abortions are the most common complication of pregnancy and nonsteroidal anti-inflammatory drugs (NSAID) are among the most widely used groups of drugs during the first trimester of pregnancy. Published data are inconsistent regarding the risk for spontaneous abortions after exposure to NSAID.

Patients (or Materials) and Methods: A population-based retrospective cohort study was conducted including all women who conceived between January 2003 and December 2009 and admitted for birth or diagnosed with spontaneous abortion at Soroka Medical Center, Clalit Health Services, Israel. A computerized database of medication dispension was linked with 2 computerized databases containing information on births and spontaneous abortions. Time-varying COX regression models were constructed adjusting for mother's age, diabetes mellitus, hypothyroidism, hypercoagulable or inflammatory conditions, history of recurrent miscarriages, presence of intrauterine contraceptive device, ethnicity, and self-reporting tobacco use during pregnancy and the year of pregnancy.

Results: There were 65,457 women who conceived during the study period and admitted at SMC: 58,949 (90.1%) for birth and 6508 (9.9%) for spontaneous abortion. A total of 4495 (6.9%) pregnant women were exposed to NSAID during the study period. Exposure to NSAID was not an independent risk factor for spontaneous abortion as groups (adjusted hazard ratio [HR], 1.08; 95% confidence interval [CI], 0.97–1.20 and adjusted HR, 1.67; 95% CI 0.95–2.95 for nonselective and selective COX2 inhibitors, respectively) or as specific drugs. Additionally, no dose response effect was found.

Conclusion: In this large population-based retrospective cohort study, no increased risk for spontaneous abortions was found following exposure to NSAID Table.

Table. The unadjusted and adjusted risk (hazard ratios and 95% CI) for spontaneous abortion following exposure to NSAID: results from time-varying multivariate Cox regression models.

	Spontaneous Abortions Hazard Ratio (95% CI)	
	Unadjusted	Adjusted*
Nonselective COX inhibitors	1.13 (1.01–1.25)	1.08 (0.97–1.20)
Ibuprofen	1.13 (0.98–1.30)	1.05 (0.92–1.21)
Diclofenac	1.21 (0.98–1.48)	1.19 (0.97–1.47)
Indomethacin	3.54 (2.20–5.71)	3.33 (2.06–5.36)
Naproxen	1.87 (0.66–1.17)	0.88 (0.66–1.18)
Etodolac	1.26 (0.88 –1.80)	0.14 (0.8–1.64)
COX2 selective inhibitors	1.97 (1.12–3.47)	1.67 (0.95–2.95)

Disclosure of Interest: None declared.

OC005—BIASES ON THE ADMINISTERED PARENTERAL DOSES OF AN EXPERIMENTAL DRUG DURING PHASE I CLINICAL TRIALS

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Introduction: The pharmaceutical aspects of drug administration in clinical trials receive poor consideration compared with the important attention devoted to the analytical and mathematical aspects